

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

CLAIMS

1-39 (Canceled)

40. (Canceled)

41-70 (Canceled)

71 (New) A method of preparing DNA fragments from a sample of nucleic acids to be analyzed, which method comprises selectively fragmenting the nucleic acids by means of at least the following steps:

a) preparing first double-stranded DNA fragments F1 using at least one type II restriction enzyme E1 which randomly fragments the sample of nucleic acids to be analyzed, and generating said DNA fragments F1 with blunt or cohesive ends;

b) obtaining DNA fragments F'1 by ligating the 5'-end of said DNA fragments F1 obtained in step a) to a first double-stranded adapter AA' so as to form a junction sequence located at the junction of the 3'-end of said first double-stranded adapter AA' and the 5'-end of said DNA fragments F1, wherein said junction sequence consists of the 5'-terminal one or more base pairs but not the entire sequence of the recognition site of a type of IIS restriction enzyme E2, the cleavage site of which is located downstream of said recognition site, and wherein said junction sequence contains at its 3'-end the 3'-terminal one or more base pairs of the E1 restriction enzyme restriction site;

- c) obtaining a fraction of short DNA fragments F2 through selective cleavage by said restriction enzyme E2, of a fraction of the DNA fragments F'1 obtained in step b) which are formed of said first double-stranded adapter AA' and the DNA fragments F1 generated in step a) whose sequence contains at its 5'-end, the sequence of the 3'-terminal one or more base pairs of the recognition site of said restriction enzyme E2, which 3'-terminal base pairs together with the 5'-terminal base pairs from said junction sequence can form the entire recognition site of the restriction enzyme E2; and
- d) purifying said fraction of short DNA fragments F2.

72. (New) The method as claimed in claim 71, wherein step a) is carried out with two different E1 restriction enzymes, E1_A and E1_C, such that:

at least one generates cohesive ends, different from those optionally generated by the other restriction enzyme, and

the E1_A has a restriction site in which the first one or more base pairs of the 3' end of the site are identical to the first base pairs only but not the entire sequence of the recognition site of the restriction enzyme E2 as defined in step b).

73. (New) The method as claimed in claim 72, wherein one of the enzymes cleaves frequently and the other rarely.

74. (New) The method as claimed in claim 73, wherein: the enzyme that cleaves frequently is the enzyme E1_A, which enzyme E1_A generates at least one end of a fragment F1 that binds to the first double-stranded adapter AA' in step b), and the enzyme that cleaves rarely,

is the enzyme E1_C which generates at least one end of a fragment F1, which binds, in step b), to a second double-stranded adapter CC' that is different from the first double-stranded adapter AA'.

75. (New) The method as claimed in claim 71, wherein steps a) and b) are carried out simultaneously.

76. (New) The method as claimed in claim 71, wherein step a) generates DNA fragments F1 of less than 1000 bp, prior to the ligation step b).

77. (New) The method as claimed in claim 71, wherein the first double-stranded adapter AA' as defined in step b) comprises, at the 3' end of the strand A or 5' end of the strand A', or both, a first sequence of approximately 1 to 8 bases or base pairs, which is partially or completely identical or complementary to the restriction site of the enzyme E1, which first sequence is chosen so as to form said junction sequence by ligation of said first double-stranded adapter AA' to the ends of said DNA fragments F1 obtained in a).

78. (New) The method as claimed in claim 77, wherein said first sequence includes one or more mismatches with the sequence of said restriction site of the restriction enzyme E1.

79. (New) The method as claimed in claim 77, wherein the first double-stranded adapter AA' comprises, upstream of the first sequence, a second sequence of at least 6 base pairs.

80. (New) The method as claimed in claim 79, wherein the first double-stranded adapter AA' comprises a first sequence which is complementary to the cohesive end which is generated by the restriction enzyme E1 and at least one base located between said first

sequence and said second sequence, wherein said base is different from that of the E1 enzyme restriction site which is immediately adjacent to said complementary sequence.

81. (New) The method as claimed in claim 71, wherein the first double-stranded adapter AA' as defined in step b) comprises a phosphate residue covalently linked to the 5' end of the strand A'.

82. (New) The method as claimed in claim 71, which further comprises at least one additional step or a combination thereof comprising amplifying the fragments F'1 or F2 using a pair of primers.

83. (New) The method as claimed in claim 71, wherein the first double-stranded adapter AA' as defined in step b) is linked, at the 5' end of its strand A, to a label.

84. (New) The method as claimed in claim 74, wherein the 5' end of the strand C' of the second double-stranded adapter CC' is linked to a label, which label is attachable to a functionalized solid support.

85. (New) The method as claimed in claim 83, wherein the fragments F'1 obtained in step b) are brought into contact with said functionalized support prior to the cleavage step c), and the fraction of short fragments F2 of step d) corresponds to the fraction of free fragments.

86. (New) The method as claimed in claim 71, which further comprises obtaining single-stranded fragments from the short DNA fragments F2.

87. (New) The method as claimed in claim 82, which further comprises purifying the amplification products of said DNA fragments F'1 or F2.

88. (New) An isolated short DNA fragment of less than 100 bases or base pairs obtained by the method as claimed in claim 71, which comprises a portion of genomic DNA or of cDNA bordered respectively by the recognition site and the cleavage site of a restriction enzyme E2 the cleavage site of which is located downstream of said recognition site, and wherein the 5' end of said genomic DNA or cDNA portion is identical to the last base pairs of the recognition site of said enzyme E2, said short DNA fragment further comprising at least 6 bases or 6 base pairs, upstream of the recognition site of the enzyme E2 and downstream of the cleavage site of said enzyme E2.

89. (New) The DNA fragment as claimed in claim 88, which is a single-stranded fragment.

90. (New) The DNA fragment as claimed in claim 88, which is linked, at one of its 5' ends, to a label.

91. (New) The method as claimed in claim 82, wherein the pair of primers are a pair of labeled primers.

92. (New) The method as claimed in claim 83, wherein the label is a label for detecting nucleic acid hybrids.

93. (New) The method as claimed in claim 83, wherein the label is attachable to a functionalized solid support.

94. (New) The method as claimed in claim 83, wherein the label which is linked to the first double-stranded adapter AA' is attachable to a functionalized support, and wherein the DNA fragments F'1 obtained in step b) are brought into contact with said functionalized support prior to the cleavage step c), and the fraction of short fragments F2 of step d) corresponds to the fraction of fragments that is retained on said support.

95. (New) The method as claimed in claim 71, which further comprises a second selection of one or more subset(s) of fragments from the fraction of short DNA fragments F2 obtained in step d) following the steps of:

- e) ligating the end of the short DNA fragments F2 obtained in d) which is not linked to the first double-stranded adapter AA' to at least a third complementary double-stranded adapter BB', thereby producing short fragments F'2; and
- f) amplifying the short DNA fragments F'2 linked to said double-stranded-adapters, using at least one pair of primers, so as to select at least one subset of short DNA fragments F'2 from the fraction of short fragments F2 obtained in d).

96. (New) The method as claimed in claim 95, wherein one of the primers of step f) is labeled at its 5' end.

97. (New) The method as claimed in claim 95, wherein step e) comprises ligating several different complementary double-stranded adapters BB', each comprising a specific sequence of 1 to 10 bases, at the 5' end of the strand B or at the 3' end of the strand B'.

98. (New) The method as claimed in claim 95, wherein said double-stranded adapter BB' of step e) comprises a phosphate residue covalently linked to the 5' end of the strand B.

99. (New) The method as claimed in claim 95, which further comprises obtaining single-stranded fragments from the short DNA fragments F'2.

100. (New) The method as claimed in claim 95, which further comprises purifying the amplification products of said short DNA fragments F'2.